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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/945,459	12/09/1997	FUSAO MAKISHIMA*	146.1275	2741

7590 10/22/2002

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EXAMINER

ROMEO, DAVID S

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/22/2002 34

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	08/945,459	MAKISHIMA ET AL.
Examiner	Art Unit	
David S Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 24 June 2002.

2a) This action is **FINAL**.      2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

4) Claim(s) 17-47 is/are pending in the application.

4a) Of the above claim(s) 29-40 is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 17-28 and 41-47 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All   b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____.
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>29</u> .	6) <input type="checkbox"/> Other: _____

### **DETAILED ACTION**

The request for a continued prosecution application (CPA) under 37 CFR 1.53(d) filed on June 24, 2002 is acknowledged. 37 CFR 1.53(d)(1) was amended to provide that the prior application of a CPA must be: (1) a utility or plant application that was filed under 35 U.S.C. 5 111(a) before May 29, 2000, (2) a design application, or (3) the national stage of an international application that was filed under 35 U.S.C. 363 before May 29, 2000. *See Changes to Application Examination and Provisional Application Practice*, interim rule, 65 Fed. Reg. 14865, 14872 (Mar. 20, 2000), 1233 Off. Gaz. Pat. Office 47, 52 (Apr. 11, 2000). Since a CPA of this application is not permitted under 37 CFR 1.53(d)(1), the improper request for a CPA is 10 being treated as a request for continued examination of this application under 37 CFR 1.114. *See id.* at 14866, 1233 Off. Gaz. Pat. Office at 48.

The amendments filed August 1, 2002 (Paper No. 33) and June 24, 2002 (Paper No. 32) have been entered. Claims 17-47 are pending. Claims 29-40 are withdrawn from further 15 consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 26. Claims 17-28, 41-47 are being examined. Any objection and/or rejection of record that is not maintained and/or repeated in this Office action is withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior 20 Office action. Citations by the examiner are in an alphanumeric format, such as "(a1)", wherein the "a" refers to the reference cited on the Notice of References Cited, PTO-892, and the "1" refers to the Paper No. to which the Notice of References Cited, PTO-892, is attached.

**Maintained Formal Matters, Objections, and/or Rejections:**

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Celeste (a10) in view of Ben-Bassat (w10), Hirel (u20), and Georgiou (x13) and further in view of Tonouchi 5 (y13) and Thompson (a27).

Claims 17, 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Celeste (a10) in view of Ben-Bassat (w10), Hirel (u20), and Georgiou (x13) and further in view of Tonouchi (y13) and Thompson (a27) as applied to claim 17 above and further in view of Hotten 10 (2, cited by Applicants) and Cerletti (n10).

Claims 17-28, 41-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Celeste (a10) in view of Ben-Bassat (w10), Hirel (u20), and Georgiou (x13) and further in view of Tonouchi (y13) and Thompson (a27) as applied to claim 17 above and further in view of Hotten 15 (2, cited by Applicants) and Cerletti (n10) as applied to claim 18 above and further in view of Neidhardt (1, cited by Applicants).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on 20 obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the

applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicants call the examiner's attention to examples 5 and 6 in Celeste (a10) and argue that this is a clear teaching that MP52 does not possess cartilage or bone formation. Applicants 5 arguments have been fully considered but they are not persuasive. Firstly, although human MP52 protein and the murine homologue of BMP-13 protein were expressed and assayed for tendon/ligament-like tissue inducing activity and all proteins showed comparable results, similar to those described for human BMP-12 (example 6) and no bone or cartilage formation was observed for all doses of BMP-12 tested (example 5) this does teach that MP52 lacks cartilage or 10 bone formation activity because it only teaches that MP52, like BMP-12, possess tendon/ligament-like tissue inducing activity. Secondly, bone or cartilage inducing activity is an intended use of the claimed compound or composition and is not considered a limitation and is of no significance to claim construction. To argue that MP52 does not possesses bone or cartilage 15 inducing activity is to argue that present specification has not enabled the intended use of the claimed compound or composition. Thirdly, Celeste's BMP-12 (SEQ ID NO: 2) and MP52 (SEQ ID NO: 4) are clearly different proteins at the amino acid level.

Applicants argue that there is no pertinent showing regarding expected activity of shortened forms of MP52. Applicants arguments have been fully considered but they are not 20 persuasive. Celeste teaches that human MP52 proteins containing the amino acid sequence from amino acid #17 or #19 to #119 or #120 of Celeste's SEQ ID NO: 4 are expected to retain activity (column 7, full paragraph 3). This is evidence that one of ordinary skill in the art would expect

the shortened forms to retain activity. Applicants have not provided evidence contrary to this teaching or expectation.

Applicants argue that there is no teaching of Applicants' method. Applicants arguments have been fully considered but they are not persuasive. The present claims are not drawn to a  
5 method but are drawn to a compound or composition.

Applicants argue that combination with the secondary and tertiary references would not point out the claimed invention to one skilled in the art. Applicants arguments have been fully considered but they are not persuasive. In expressing mature MP52 in bacteria one of ordinary skill in the art would reasonably expect to obtain mature MP52 with the following N-terminal  
10 amino acid sequences, according to the teachings of Ben-Bassat and Hirel: Met-Ala-Pro, Ala-Pro, and Pro. Ben-Bassat also suggest obtaining a homogeneous protein product without the N-terminal methionine; purified MAP could be used to "polish" the frayed amino terminal sequences (page 756, paragraph bridging columns 1-2). Thompson at the paragraph bridging columns 1-2 teaches that it is generally considered desirable for clinical use to obtain a  
15 homogeneous material, i.e. a protein having essentially the same N-terminal sequence from molecule to molecule. Tonouchi provides the means to obtain from a mixture of MP52 proteins having heterogeneous termini a MP52 protein having essentially the same N-terminal sequence from molecule to molecule, which the references clearly suggest. Sherman and Georgiou are evidence of the principles, namely, retention of the N-terminal methionine and desirability of its  
20 removal, known to one of ordinary skill, that suggests the claimed combination.

**New formal matters, objections, and/or rejections:**

***Information Disclosure Statement***

The references lined through on the information disclosure statement filed on November 12, 2001 (Paper No. 29) do not fully comply with the requirements of 37 CFR 1.98 because: it 5 does not identify each publication listed by publisher, author (if any), title, relevant pages of the publication, date, and place of publication, as required by 37 CFR § 1.98 (b)(5). The submission appears to be *bona fide*. Failure to timely comply with this notice will result in the above mentioned information disclosure statement being placed in the application file with the noncomplying information **not** being considered. See 37 CFR 1.97(i).

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***Conclusion***

No claims are allowable.

15 ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

20 BEFORE FINAL (703) 872-9306  
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FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

30



DAVID ROMEO  
PRIMARY EXAMINER  
ART UNIT 1647

DSR  
OCTOBER 21, 2002